REMARKS/ARGUMENTS

The Examiner has rejected Claims 1-17 under 35 U.S.C. 103(a) as being unpatentable over Lubitz (http://www.allergytriggers.com/treatments/medications/nose/allegra.htm) in view of Chhabra et al. (6,500,459). The Examiner states that it would have been obvious to have prepared a pharmaceutical composition comprising fexofenadine HCl, lactose and hydroxypropyl cellulose of different wt. % to be used as an antihistamine composition, since Chhabra et al. disclose that hydroxypropyl cellulose can be used in place of microcrystalline cellulose.

Lubitz teaches Allegra ® capsules which are available from Aventis containing fexofenadine hydrochloride, croscarmellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch. Thus, the Allegra® capsules do not contain a low-substituted hydroxypropyl cellulose.

Chhabra teaches a sustained release pharmaceutical composition comprising a core and a functional coating membrane surrounding the core. The core comprises an active ingredient, a hydrophilic carrier, a hydrodynamic diffusion enhancer, and conventional pharmaceutical excipients. Chhabra lists hydroxypropyl cellulose as an example of a hydrophilic carrier (col. 9, line 13) and as an example of a filler and binder (col. 10, line 14). Chhabra does not teach or suggest low-substituted hydroxypropyl cellulose. Moreover, none of Chhabra's examples use either lactose or a low-substituted hydroxypropyl cellulose.

It is noted that the *Handbook of Pharmaceutical Excipients*, Fourth Edition, Rowe, Sheskey, and Weller, (2003), has separate chapters for hydroxypropyl cellulose and low-substituted hydroxypropyl cellulose. As stated in the *Handbook of Pharmaceutical Excipients*, on page 294, the low-substituted hydroxypropyl cellulose when dried at 105 °C for 1 hour contains not less than 5% and not more than 16% of hydroxypropoxy groups. In contrast, hydroxypropyl cellulose is defined by a molecular weight range of 50,000 to 1,250,000 according to the *Handbook of Pharmaceutical Excipients*, page 289. Thus, the low-substituted hydroxypropyl cellulose is clearly distinguishable from hydroxypropyl cellulose.

Applicants unexpectedly determined that tablets prepared with lactose and a low-substituted hydroxypropyl cellulose exhibited a significantly greater bioavailability as determined by AUC and C_{max}, than tablets comprising fexofenadine and fillers other than lactose, and disintegrants other than low-substituted hydroxypropyl cellulose. For example, applicants prepared two similar tablet compositions in Examples 1 and 2 of the specification. The tablets prepared in Example 1 contained lactose and a low-substituted hydroxypropyl cellulose. The tablets prepared in Example 2 contained mannitol and polacrilin potassium.

The tablets prepared in Examples 1 and 2 were evaluated in a bioavailability study which is described in applicants' specification in Example 3. As stated in Example 3, the bioavailability was measured in a total of 32 patients who were dosed with the tablets prepared in Example 1 or the tablets prepared in Example 2. Thus, 16 patients received one tablet prepared in Example 1, and 16 patients received one tablet prepared in Example 2. In addition each patent received a reference tablet of Allegra ® which is a film coated tablet available from Aventis containing fexofenadine hydrochloride, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and pregelatinized starch (the Allegra® tablet does not contain lactose or low-substituted hydroxypropyl cellulose).

An interval of at least 7 days existed between each patient study. Plasma samples were taken in each patent over a period of 60 hours at time intervals of 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 10, 12, 18, 24, 30, 36, 48, and 60 hours. The plasma samples were analyzed for the plasma concentration of fexofenadine. The data was expressed as C_{max}, the maximum amount of fexofenadine found in the plasma, and as AUC, the area under the plasma concentration time curve.

The results of applicants' bioavailability study shows that the tablets prepared in Example 1 which were prepared with lactose and low-substituted hydroxypropyl cellulose exhibited a significantly greater bioavailability as determined by AUC and C_{max}, as compared to the tablets prepared in Example 2 which were prepared with mannitol and polacrilin potassium. In addition, the results in Table I show that the tablets prepared in Example 1 were bioequivalent to the reference product Allegra®.

The combination of Lubitz and Chhabra, therefore, does not place one skilled in the art in possession of applicants' invention as claimed because neither Lubitz nor Chhabra teach a fexofenadine composition containing a low-substituted hydroxypropyl cellulose. In addition, neither reference teaches a fexofenadine composition comprising a combination of lactose and a low-substituted hydroxypropyl cellulose, as claimed by applicants.

The Examiner has rejected Claims 18-20 under 35 U.S.C. 103(a) as being unpatentable over Chhabra et al. (US 6,500,459 B1). The Examiner states that it would have been obvious to have used the method of Chhabra to prepare a pharmaceutical composition comprising fexofenadine, lactose and hydroxypropyl cellulose of different wt. % to be used as an antihistamine.

As noted above, applicants unexpectedly determined that tablets prepared with lactose and a low-substituted hydroxypropyl cellulose exhibited a significantly greater bioavailability as determined by AUC and C_{max}, than tablets comprising fexofenadine and fillers other than lactose, and disintegrants other than low-substituted hydroxypropyl cellulose.

Chhabra lists hydroxypropyl cellulose as an example of a hydrophilic carrier (col. 9, line 13) and as an example of a filler and binder (col. 10, line 14). Chhabra does not teach or suggest low-substituted hydroxypropyl cellulose. Moreover, none of Chhabra's examples use either lactose or a low-substituted hydroxypropyl cellulose. In addition, it was explained above that low-substituted hydroxypropyl cellulose is clearly distinguishable from hydroxypropyl cellulose.

Thus, Chhabra does not place one skilled in the art in possession of applicants' invention as claimed because Chhabra does not teach or suggest a fexofenadine composition which has significantly improved bioavailability as determined by AUC and C_{max} due to the presence of lactose and a low-substituted hydroxypropyl cellulose, as prepared by applicants' claimed process.

It is requested that the Examiner reconsider the rejections in view of the remarks and pass the case to issue.

Enclosed is a Fee Letter and Supplemental Information Disclosure Statement.

Respectfully submitted,

Novartis
Corporate Intellectual Property
One Health Plaza, Building 430
East Hanover, NJ 07936-1080
(862) 778-7945

John D. Thallemer
Attorney for Applicants
Reg. No. 34,940

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